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(FILE 'HOME' ENTERED AT 17:38:04 ON 07 JUL 2003)

FILE 'MEDLINE' ENTERED AT 17:38:13 ON 07 JUL 2003

L1 3 S THREONINE(3A)274  
L2 1 S VALINE(3A)274  
L3 0 S L1 AND L2  
L4 4 S L1 OR L2

FILE 'MEDLINE, SCISEARCH, EMBASE, CAPLUS, BIOSIS, LIFESCI, CONFSCI'  
ENTERED AT 17:42:15 ON 07 JUL 2003

L5 19 S L1  
L6 19 S THREONINE(3A)274  
L7 11 S VALINE(3A)274  
L8 1 S L1 AND L2  
L9 29 S L1 OR L2  
L10 0 S L9 NOT L4

FILE 'WPIDS' ENTERED AT 17:45:45 ON 07 JUL 2003

L11 1 S L5  
L12 1 S L6  
L13 0 S L7

FILE 'USPATFULL' ENTERED AT 17:47:05 ON 07 JUL 2003

L14 83 S L6  
L15 10 S L7  
L16 2 S L1 AND L2  
L17 91 S L1 OR L2

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L8 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2003 THOMSON ISI  
AN 2003:452849 SCISEARCH  
GA The Genuine Article (R) Number: 658QZ  
TI Functional expression of a **valine-274** to  
**threonine** mutation (V274T) in rat alpha 7 nicotinic acetylcholine  
receptors (nAChR) in recombinant GH4C1 cells  
AU David J (Reprint); Misner D; Martin R; Nguyen D; Lansing C; Madden F;  
Dietrich P; Vivian J; Bonhaus D  
CS Roche Biosci, CNS Neurobiol Unit, Palo Alto, CA 94304 USA  
CYA USA  
SO FASEB JOURNAL, (14 MAR 2003) Vol. 17, No. 4, Part 1, Supp. [S], pp.  
A627-A627.  
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD  
20814-3998 USA.  
ISSN: 0892-6638.  
DT Conference; Journal  
LA English  
REC Reference Count: 0

L4 ANSWER 1 OF 4 MEDLINE  
 AN 1999180249 MEDLINE  
 DN 99180249 PubMed ID: 10082212  
 TI Gain of function mutation of the alpha7 nicotinic receptor: distinct pharmacology of the human alpha7V274T variant.  
 AU Briggs C A; McKenna D G; Monteggia L M; Touma E; Roch J M; Arneric S P; Gopalakrishnan M; Sullivan J P  
 CS Neuroscience Research, Abbott Laboratories, Abbott Park, IL 60064, USA.. clark.briggs@abbott.com  
 SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1999 Feb 5) 366 (2-3) 301-8. Journal code: 1254354. ISSN: 0014-2999.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199904  
 ED Entered STN: 19990511  
 Last Updated on STN: 19990511  
 Entered Medline: 19990427  
 AB In the human alpha7 nicotinic receptor, **valine-274** in the pore-lining transmembrane-2 region was mutated to threonine to produce the variant human alpha7V274T, which was evaluated electrophysiologically following expression in *Xenopus laevis* oocytes. Inward current rectification was strong in human alpha7V274T as in the human alpha7 wild type nicotinic receptor. However, human alpha7V274T was 100-fold more sensitive to the nicotinic receptor agonists acetylcholine, (-)-nicotine and 1,1-dimethyl-4-phenylpiperazinium. Choline also activated human alpha7V274T (EC50 = 12 microM) and was 82-fold more potent than at human alpha7 wild type nicotinic receptor. (-)-Cotinine, (2,4)-dimethoxybenzylidene anabaseine (GTS-21) and 2-methyl-3-(2-(S)-pyrrolidinylmethoxy)pyridine (ABT-089), weak partial agonists at human alpha7 wild type, were much stronger agonists at human alpha7V274T with EC50 values of 70 microM, 4 microM and 28 microM and fractional activation values of 93%, 96% and 40%, respectively. However, (-)-lobeline, a human alpha7 wild type nicotinic receptor antagonist, and dihydro-beta-erythroidine, which activates chick mutagenized alpha7 nicotinic receptors, had only weak agonist-like activity at human alpha7V274T (< or = 4% of the maximal acetylcholine response). Methylllycaconitine, mecamlamine, d-tubocurarine and dihydro-beta-erythroidine retained antagonist activity and, indeed, appeared to be at least as potent at human alpha7V274T as at human alpha7 wild type. These results support and extend the concept that human nicotinic receptor pharmacology can be profoundly altered by single amino acid changes in the pore-lining segment.